

FILE 'REGISTRY' ENTERED AT 16:47:32 ON 23 JUN 2008  
L1 STRUCTURE UPLOADED  
L2 0 S L1  
L3 STRUCTURE UPLOADED  
L4 5 S L3  
L5 125 F L3 SSS FULL

FILE 'CAPLUS' ENTERED AT 16:50:02 ON 23 JUN 2008  
L6 11 S L5

FILE 'REGISTRY' ENTERED AT 17:08:00 ON 23 JUN 2008  
L7 STRUCTURE UPLOADED  
L8 11 S L7  
L9 209 S L7 SSS FULL

FILE 'CAPLUS' ENTERED AT 17:08:36 ON 23 JUN 2008  
L10 3 S L9

=> file registry  
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.21	0.21

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 16:47:32 ON 23 JUN 2008  
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STRUCTURE FILE UPDATES: 22 JUN 2008 HIGHEST RN 1029806-10-7  
DICTIONARY FILE UPDATES: 22 JUN 2008 HIGHEST RN 1029806-10-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

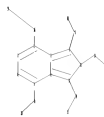
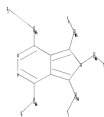
Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and  
predicted properties as well as tags indicating availability of  
experimental property data in the original document. For information  
on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stdoc/properties.html>

=>

Uploading C:\Program Files\STNEXP\Queries\10520962generic.str



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chain nodes :
10 11 14 15 16 17 18 19 20 21
ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
2-16 5-15 7-17 8-10 9-14 10-11 14-21 15-20 16-19 17-18
ring bonds :
1-2 1-6 2-3 3-4 3-7 4-5 4-9 5-6 7-8 8-9
exact/norm bonds :
1-2 1-6 2-3 3-4 3-7 4-5 4-9 5-6 7-8 8-9 8-10 10-11 14-21 15-20 16-19
17-18
exact bonds :
2-16 5-15 7-17 9-14

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G1:H,Cy

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Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS

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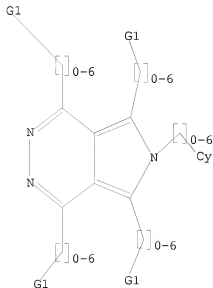
11:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS  
21:CLASS

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



G1 H,Cy

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 16:47:55 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 94453 TO ITERATE

2.1% PROCESSED 2000 ITERATIONS

0 ANSWERS

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*INCOMPLETE\*\*

BATCH \*\*INCOMPLETE\*\*

PROJECTED ITERATIONS: 1870802 TO 1907318

PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=>

Uploading C:\Program Files\STNEXP\Queries\10520962simple.str



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chain nodes :
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ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
2-16 5-15 7-17 8-10 9-14 10-11
ring bonds :
1-2 1-6 2-3 3-4 3-7 4-5 4-9 5-6 7-8 8-9
exact/norm bonds :
1-2 1-6 2-3 2-16 3-4 3-7 4-5 4-9 5-6 5-15 7-8 7-17 8-9 8-10 9-14
10-11

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G1:H,C

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Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS

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L3 STRUCTURE UPLOADED

=> s l3

SAMPLE SEARCH INITIATED 16:49:18 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 6814 TO ITERATE

29.4% PROCESSED 2000 ITERATIONS

5 ANSWERS

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

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PROJECTED ANSWERS: 93 TO 587

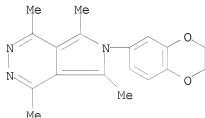
L4 5 SEA SSS SAM L3

=> d l4 scan

L4 5 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN

IN 6H-Pyrrolo[3,4-d]pyridazine, 6-(2,3-dihydro-1,4-benzodioxin-6-yl)-1,4,5,7-tetramethyl-

MF C18 H19 N3 O2



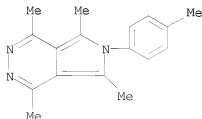
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

L4 5 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN

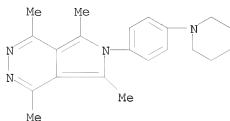
IN 6H-Pyrrolo[3,4-d]pyridazine, 1,4,5,7-tetramethyl-6-(4-methylphenyl)-

MF C17 H19 N3



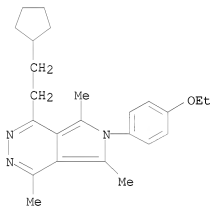
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 5 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN  
IN 6H-Pyrrolo[3,4-d]pyridazine, 1,4,5,7-tetramethyl-6-[4-(1-  
piperidinyl)phenyl]-  
MF C21 H26 N4



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

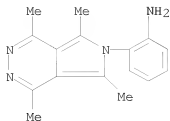
L4 5 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN  
IN 6H-Pyrrolo[3,4-d]pyridazine, 1-(2-cyclopentylethyl)-6-(4-ethoxyphenyl)-  
4,5,7-trimethyl-  
MF C24 H31 N3 O



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L4 5 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN  
IN Benzenamine, 2-(1,4,5,7-tetramethyl-6H-pyrrolo[3,4-d]pyridazin-6-yl)-  
MF C16 H18 N4



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

ALL ANSWERS HAVE BEEN SCANNED

=> f 13 sss full

FULL SEARCH INITIATED 16:49:40 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 134102 TO ITERATE

100.0% PROCESSED 134102 ITERATIONS

125 ANSWERS

SEARCH TIME: 00.00.02

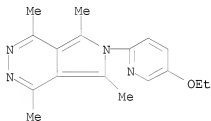
L5 125 SEA SSS FUL L3

=> d 15 scan

L5 125 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN

IN 6H-Pyrrolo[3,4-d]pyridazine, 6-(5-ethoxy-2-pyridinyl)-1,4,5,7-tetramethyl-

MF C17 H20 N4 O



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

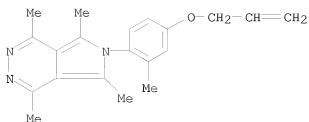
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

L5 125 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN

IN 6H-Pyrrolo[3,4-d]pyridazine, 1,4,5,7-tetramethyl-6-[2-methyl-4-(2-propen-1-yloxy)phenyl]-

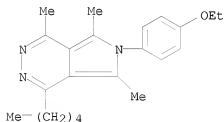
MF C20 H23 N3 O





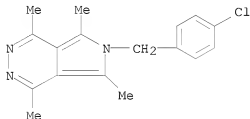
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L5 125 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN  
 IN 6H-Pyrrolo[3,4-d]pyridazine, 6-(4-ethoxyphenyl)-1,5,7-trimethyl-4-pentyl-  
 MF C22 H29 N3 O



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L5 125 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN  
 IN 6H-Pyrrolo[3,4-d]pyridazine, 6-[(4-chlorophenyl)methyl]-1,4,5,7-tetramethyl-  
 MF C17 H18 Cl N3



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus		
COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	179.74	179.95

FILE 'CAPLUS' ENTERED AT 16:50:02 ON 23 JUN 2008  
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FILE COVERS 1907 - 23 Jun 2008 VOL 148 ISS 26  
 FILE LAST UPDATED: 22 Jun 2008 (20080622/ED)

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<http://www.cas.org/legal/infopolicy.html>

=> s 15

L6 11 L5

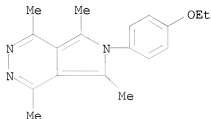
=> d 16 1-11 ti abs bib hitstr

L6 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2008 ACS ON STN  
 TI Expedited SAR study of high-affinity ligands to the  $\alpha 2\delta$  subunit of voltage-gated calcium channels: Generation of a focused library using a solution-phase Sn2Ar coupling methodology  
 AB The SAR of the lead compound 3, a novel ligand for the  $\alpha 2\delta$  subunit of voltage-gated calcium channels, was rapidly explored. Utilizing a parallel solution-phase Sn2Ar coupling approach, a focused library was obtained. The library was evaluated in vitro and afforded a series of analogs with improved potencies. The SAR trends of the library are also described.  
 AN 2005:1342000 CAPLUS <<LOGINID:20080623>>  
 DN 144:100381  
 TI Expedited SAR study of high-affinity ligands to the  $\alpha 2\delta$  subunit of voltage-gated calcium channels: Generation of a focused library using a solution-phase Sn2Ar coupling methodology  
 AU Chen, Chixu; Stearns, Brian; Hu, Tao; Anker, Naomi; Santini, Angelina; Arruda, Jeannie M.; Campbell, Brian T.; Datta, Purabi; Aiyar, Jayashree; Munoz, Benitio  
 CS Department of Chemistry, Merck Research Laboratories, San Diego, CA, 92121, USA  
 SO Bioorganic & Medicinal Chemistry Letters (2006), 16(3), 746-749  
 CODEN: BMCLE8; ISSN: 0960-894X  
 PB Elsevier B.V.  
 DT Journal  
 LA English  
 OS CASREACT 144:100381  
 IT 461432-09-7

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(SAR of high-affinity ligands to  $\alpha 2\delta$  subunit of  
voltage-gated calcium channels: generation of focused library using  
solution-phase  $S_n2Ar$  coupling methodol.)

RN 461432-09-7 CAPLUS

CN 6H-Pyrrolo[3,4-d]pyridazine, 6-(4-ethoxyphenyl)-1,4,5,7-tetramethyl- (CA  
INDEX NAME)

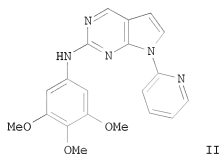
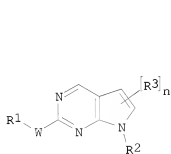


RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

TI Preparation of substituted pyrrolo[2,3-d]pyrimidines as inducers of  
keratinocyte differentiation

GI



AB The invention provides compds. I [ $n = 0-2$ ;  $W = NR_4, S, O, SO, SO_2$  (wherein  
 $R_4 = H, alkyl$ );  $R_1 = arylalkyl, heteroarylalkyl, cycloalkylalkyl, etc.$ ;  $R_2$   
 $= arylalkyl, heteroarylalkyl, cycloalkylalkyl, etc.$ ;  $R_3 = halo, OH, XSR_5,$   
 $etc.$  ( $X = a bond, alkylene$ ;  $R_5 = H, alkyl, cycloalkylalkyl$ )],  
pharmaceutical compns. comprising such compds. and methods of using such  
compds. to induce undifferentiated keratinocytes to differentiate into  
terminally differentiated keratinocytes. The invention further provides  
compds. for the treatment of diseases or disorders associated with casein  
kinase II (CK2), TANK-binding kinase 1 (TBK1) and NIMA-related kinase 9  
(NEK9). Over 200 compds. I were prepared E.g., a 4-step synthesis of II,  
starting from 5-bromo-2,4-dichloropyrimidine, was given.

AN 2005:1220346 CAPLUS <<LOGINID:20080623>>

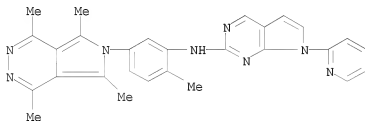
DN 143:477978

TI Preparation of substituted pyrrolo[2,3-d]pyrimidines as inducers of

keratinocyte differentiation  
 IN Hong, Jiyong; Gray, Nathanael S.; Schultz, Peter  
 PA IRM LLC, Bermuda  
 SO PCT Int. Appl., 53 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

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	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI US 2004-567346P P 20040430  
 OS CASREACT 143:477978; MARPAT 143:477978  
 IT 863597-72-2P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of substituted pyrrolo[2,3-d]pyrimidines as inducers of keratinocyte differentiation)  
 RN 863597-72-2 CAPLUS  
 CN 7H-Pyrrolo[2,3-d]pyrimidin-2-amine, N-[2-methyl-5-(1,4,5,7-tetramethyl-6H-pyrrolo[3,4-d]pyridazin-6-yl)phenyl]-7-(2-pyridinyl)- (CA INDEX NAME)



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2008 ACS ON STN  
 TI Preparation of pyrrolopyrimidines and their analogs as protein kinase inhibitors  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The invention provides a novel class of compds. I-V [n = 0-2; m = 0-3; W =

NR4, S, O, SO, SO2 (wherein R4 = H, alkyl); R1 = (un)substituted (hetero)arylalkyl, (hetero)cycloalkyl; R2 = (un)substituted (hetero)arylalkyl, (hetero)cycloalkyl; R3 = halo, OH, XSR5, etc. (X = a bond, alkylene; R5 = H, alkyl, cycloalkylalkyl)), pharmaceutical compns. comprising such compds. and methods of using such compds. to treat or prevent diseases or disorders associated with abnormal or deregulated kinase activity, particularly diseases or disorders that involve abnormal activation of the FAK, Abl, BCR-Abl, PDGF-R, c-Kit, NPM-ALK, Flt-3, JAK2 and c-Met kinases. Over 200 compds. I-V were prepared and characterized. The preparation of the compds. I is illustrated in examples. E.g., synthesis of I [R1 = 3,4,6-(MeO)3C6H2; R2 = 2-pyridyl; R3 = H; W = NH], starting from 5-bromo-2,4-dichloropyrimidine, was given. The compds. I-V were tested against various kinases. For example, they inhibit the enzyme activity by 50% (IC50), in a concentration of from 0.001 to 0.5 µM, especially from

0.01 to 0.1 µM.

AN 2005:962258 CAPLUS <<LOGINID::20080623>>

DN 143:266947

TI Preparation of pyrrolopyrimidines and their analogs as protein kinase inhibitors

IN Choi, Ha-Soon; Wang, Zhicheng; Gray, Nathanael Schiander; Gu, Xiang-Ju; He, Xiaohui; He, Yun; Jiang, Tao; Liu, Yi; Richmond, Wendy; Sim, Taebo; Yang, Kunyong

PA IRM LLC, Bermuda

SO PCT Int. Appl., 63 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

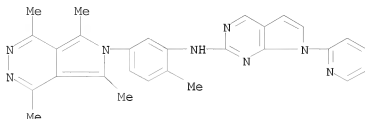
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PI	WO 2005080393	A1	20050901	WO 2005-US4630	20050214
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	RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	AU 2005214352	A1	20050901	AU 2005-214352	20050214
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	EP 1713806	A1	20061025	EP 2005-713510	20050214
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	BR 2005007668	A	20070717	BR 2005-7668	20050214
	JP 2007522241	T	20070809	JP 2006-553321	20050214
	MX 2006PA09158	A	20061110	MX 2006-PA9158	20060811
	IN 2006CN02987	A	20070608	IN 2006-CN2987	20060814
	US 20070225306	A1	20070927	US 2007-589099	20070611
PRAI	US 2004-544944P	P	20040214		
	WO 2005-US4630	W	20050214		
OS	MARPAT 143:266947				
IT	863597-72-2P				

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn of pyrrolopyrimidines and their analogs as protein kinase inhibitors)

RN 863597-72-2 CAPLUS

CN 7H-Pyrrolo[2,3-d]pyrimidin-2-amine, N-[2-methyl-5-(1,4,5,7-tetramethyl-6H-pyrrolo[3,4-d]pyridazin-6-yl)phenyl]-7-(2-pyridinyl)- (CA INDEX NAME)

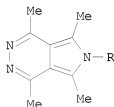


RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

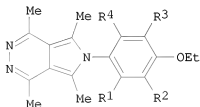
L6 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2008 ACS ON STN

TI Synthesis and biological evaluation of 6-aryl-6H-pyrrolo[3,4-d]pyridazine derivatives as high-affinity ligands of the  $\alpha 2\delta$  subunit of voltage-gated calcium channels

GI



I



II

AB 2H-pyrrolo[3,4-c]pyridazines I (R = 4-EtOC6H4, 2-EtO-5-pyridinyl, 5-EtO-2-pyridinyl, 5-EtO-2-pyrazinyl, 4-EtO-1-pyridazinyl, 2-EtO-5-pyrimidinyl, etc.) such as II (R1 = H, MeO, Et, H2C:CH, Me, MeS, EtO, F; R2 = H, Me; R3 = H, Me, Cl, HOCH2; R4 = H, Me) are prepared as ligands for the  $\alpha 2\delta$  subunit of voltage-gated calcium channels. Ortho-substituents capable of electron-donation increase the binding of II to the  $\alpha 2\delta$  subunit of voltage-gated calcium channels; electron-withdrawing substituents in the ortho-position of II decrease binding significantly. II (R1 = MeO; R2 = R3 = R4 = H) binds to the  $\alpha 2\delta$  subunit of voltage-gated calcium channels from A710 cells with an IC50 value of 4 nM. Testing of tritiated ligand II (R1 = TCH2TCH; R2 = R3 = R4 = H) in purified human  $\alpha 2\delta$  voltage-gated calcium channel subunits indicates that II displace Gabapentin from the  $\alpha 2\delta$  subunit of voltage-gated calcium channels, and thus act as Gabapentin mimics in vitro. In the preparation of II (R1 = Et; R2 = R3 = R4 = H), a novel metal-free hydrogenation is used using hydrazine as the reductant; the reduction is effective in other systems (no data).

AN 2004:303255 CAPLUS <<LOGINID::20080623>>

DN 141:54277

TI Synthesis and biological evaluation of 6-aryl-6H-pyrrolo[3,4-d]pyridazine derivatives as high-affinity ligands of the  $\alpha_2\delta$  subunit of voltage-gated calcium channels

AU Hu, Tao; Stearns, Brian A.; Campbell, Brian T.; Arruda, Jeannie M.; Chen, Chixu; Aiyar, Jayashree; Bezverkov, Robert E.; Santini, Angelina; Schaffhauser, Herve; Liu, Wensheng; Venkatraman, Shankar; Munoz, Benito

CS MRLSDB2, Department of Medicinal Chemistry, Merck Research Laboratories, San Diego, CA, 92121, USA

SO Bioorganic & Medicinal Chemistry Letters (2004), 14(9), 2031-2034  
CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier Science B.V.

DT Journal

LA English

OS CASREACT 141:54277

IT 647845-61-2P 647845-62-3P 706822-55-1P  
706822-56-2P 706822-57-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(heteroaryl-substituted pyrrolo[3,4-c]pyridazines are less effective ligands than aryl-substituted pyrrolo[3,4-c]pyridazines for the  $\alpha_2\delta$  subunit of voltage-gated calcium channels)

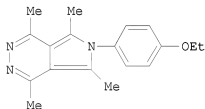
RN 647845-61-2 CAPLUS

CN 6H-Pyrrolo[3,4-d]pyridazine, 6-(6-ethoxy-3-pyridinyl)-1,4,5,7-tetramethyl-  
(CA INDEX NAME)

L6 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

TI Synthesis and biological evaluation of 6-aryl-6H-pyrrolo[3,4-d]pyridazine derivatives: high-affinity ligands to the  $\alpha_2\delta$  subunit of voltage gated calcium channels

GI

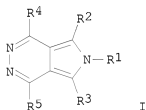


I

AB A novel class of 6-aryl-6H-pyrrolo[3,4-d]pyridazine ligands for the  $\alpha_2\delta$  subunit of voltage-gated calcium channels has been described. Substitutions in the aryl ring of the mol. were generally not tolerated, and resulted in diminished binding to the  $\alpha_2\delta$  subunit. Modifications to the pyridazine ring revealed numerous permissive substitutions, and detailed SAR studies were carried out in this portion of the mol. Replacement of the pyridazine ring Me group with an aminomethyl functionality provided greatly improved potency over the initial lead. The initial lead compound (I) displayed good rat pharmacokinetic properties, and was shown to be efficacious in the Chung model for neuropathic pain in rats.

AN 2004:153601 CAPLUS <<LOGINID::20080623>>  
DN 140:357282

TI Synthesis and biological evaluation of 6-aryl-6H-pyrrolo[3,4-d]pyridazine derivatives: high-affinity ligands to the  $\alpha_2\delta$  subunit of voltage gated calcium channels  
 AU Stearns, Brian A.; Anker, Naomi; Arruda, Jeannie M.; Campbell, Brian T.; Chen, Chixu; Cramer, Merryl; Hu, Tao; Jiang, Xiaohui; Park, Kenneth; Ren, Kun Kun; Sablad, Marciano; Santini, Angelina; Schaffhauser, Herve; Urban, Mark O.; Munoz, Benito  
 CS Department of Medicinal Chemistry, Merck Research Laboratories, San Diego, CA, 92121, USA  
 SO Bioorganic & Medicinal Chemistry Letters (2004), 14(5), 1295-1298  
 CODEN: BMCLE8; ISSN: 0960-894X  
 PB Elsevier Science B.V.  
 DT Journal  
 LA English  
 OS CASREACT 140:357282  
 IT 461432-09-7  
 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); BIOL (Biological study)  
 (preparation of 6-aryl-6H-pyrrolo[3,4-d]pyridazine derivs. as high-affinity ligands to the  $\alpha_2\delta$  subunit of voltage gated calcium channels)  
 RN 461432-09-7 CAPLUS  
 CN 6H-Pyrrolo[3,4-d]pyridazine, 6-(4-ethoxyphenyl)-1,4,5,7-tetramethyl- (CA INDEX NAME)  
 L6 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Treatment of neuropathic pain with 6H-pyrrolo[3,4-d]pyridazine compounds  
 GI



AB The title compds. [I; R1 = (un)substituted alkyl(hetero)aryl, alkyl(hetero)cycloalkyl, (hetero)aryl, (hetero)cycloalkyl; R2-R5 = a bond, (un)substituted alkyl, alkyl(hetero)aryl, alkyl(hetero)cycloalkyl, (hetero)aryl, (hetero)cycloalkyl] were prepared as ligands of voltage gated calcium channels (VGCC), useful in the treatment of neuropathic pain, and psychiatric and mood disorders such as, for example, schizophrenia, anxiety, depression, panic, and bipolar disorder, as well as in the treatment of pain, Parkinson's disease, cognitive dysfunction, epilepsy, circadian rhythm disorders, drug addiction, drug abuse, drug withdrawal and other. E.g., a multi-step synthesis of I [R1 = 4-EtOC6H4; R2-R4 = Me; R5 = 4-MeOC6H4] which produced a 65% effect after i.p. dosing at 30 mg/kg in spinal nerve ligation model of neuropathic pain in rats, was given. The pharmaceutical composition comprising the compound I is claimed.  
 AN 2004:60243 CAPLUS <<LOGINID::20080623>>  
 DN 140:111422  
 TI Treatment of neuropathic pain with 6H-pyrrolo[3,4-d]pyridazine compounds  
 IN Anker, Naomi Burke; Arruda, Jeannie M.; Campbell, Brian Thomas; Munoz,



Benito; Prasit, Petpiboon; Stearns, Brian A.  
 PA Merck & Co., Inc., USA  
 SO PCT Int. Appl., 203 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004006836	A2	20040122	WO 2003-US21493	20030708
	WO 2004006836	A3	20040415		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CA 2492022	A1	20040122	CA 2003-2492022	20030708
	AU 2003248907	A1	20040202	AU 2003-248907	20030708
	AU 2003248907	B2	20070426		
	EP 1539168	A2	20050615	EP 2003-764414	20030708
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
	JP 2005536507	T	20051202	JP 2004-521592	20030708
	US 20060154929	A1	20060713	US 2005-520962	20051128
PRAI	US 2002-394734P	P	20020711		
	WO 2003-US21493	W	20030708		
OS	MARPAT 140:111422				
IT	647845-41-8P 647845-64-5P 647845-85-0P				
	647845-88-3P 647845-89-4P 647845-90-7P				
	RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)				
	(preparation of 6H-pyrrolo[3,4-d]pyridazines for treating neuropathic pain)				
RN	647845-41-8 CAPLUS				
CN	6H-Pyrrolo[3,4-d]pyridazine-1-propanoic acid, 6-(4-ethoxyphenyl)-4,5,7-trimethyl-, methyl ester (CA INDEX NAME)				

L6 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Synthesis and electrophilic substitution of dipyrrolo[1,2-b:3,4-d]pyridazines  
 AB Dipyrrolo[1,2-b:3,4-d]pyridazines were prepared from 1,4,5,7-tetramethyl-6-R1-pyrrolo[3,4-d]pyridazines. The dipyrrolo[1,2-b:3,4-d]pyridazines were found to have high nucleophilicity and electrophilic substitution occurs at C7, or C7 and C9 depending on the steric bulk and activity of the attacking electrophile.  
 AN 2003:927977 CAPLUS <<LOGINID::20080623>>  
 DN 140:303615  
 TI Synthesis and electrophilic substitution of dipyrrolo[1,2-b:3,4-d]pyridazines  
 AU Arsen'ev, V. G.; Arsen'eva, M. Yu.; Shopin, D. V.; Olekhovich, L. P.  
 CS Rostov State University, Rostov-on-Don, 344006, Russia  
 SO Chemistry of Heterocyclic Compounds (New York, NY, United States)(Translation of Khimiya Geterotsiklicheskh Soedinenii) (2003), 39(5), 669-670

CODEN: CHCCAL; ISSN: 0009-3122

PB Kluwer Academic/Consultants Bureau

DT Journal

LA English

OS CASREACT 140:303615

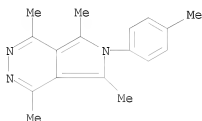
IT 378216-53-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(synthesis of dipyrrolopyridazines from pyrrolopyridazines and their reactivity in electrophilic substitution reactions)

RN 378216-53-6 CAPLUS

CN 6H-Pyrrolo[3,4-d]pyridazine, 1,4,5,7-tetramethyl-6-(4-methylphenyl)- (CA INDEX NAME)

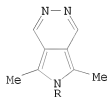


RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

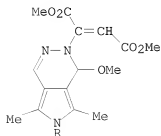
L6 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

TI Pyrrole studies. Part 32. A novel ring-cleavage reaction of the pyridazine ring during the reaction of 6H-pyrrolo[3,4-d]pyridazines with dimethyl acetylenedicarboxylate

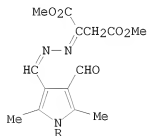
GI



I



II



III

AB Treatment of pyrrolopyridazines I (R = Me, H, Ph) with (MeO2CC.tplbond.)2 in MeOH at -70° gave the corresponding esters II (R as before), which were unstable in the presence of H2O and underwent ring cleavage to

the corresponding pyrroles III. The structure of III (R = H) was confirmed by x-ray anal.

AN 1985:471267 CAPLUS <<LOGINID::20080623>>

DN 103:71267

OREF 103:11469a,11472a

TI Pyrrole studies. Part 32. A novel ring-cleavage reaction of the pyridazine ring during the reaction of 6H-pyrrolo[3,4-d]pyridazines with dimethyl acetylenedicarboxylate

AU Hernandez de la Figuera Gomez, Teresa; Sepulveda Arques, Jose; Jones, R. Alan; Dawes, Helen M.; Hursthouse, Michael B.

CS Dep. Quim. Org., Univ. Valencia, Valencia, Spain

SO Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1985), (4), 899-902

CODEN: JCPRB4; ISSN: 0300-922X

DT Journal

LA English

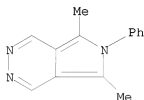
OS CASREACT 103:71267

IT 97476-49-8

RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with di-Me acetylenedicarboxylate)

RN 97476-49-8 CAPLUS

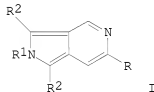
CN 6H-Pyrrolo[3,4-d]pyridazine, 5,7-dimethyl-6-phenyl- (CA INDEX NAME)



L6 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

TI Structure and reactivity of iso-fused heterocyclic systems with  $4n\pi$  and  $(4n+2)\pi$  electrons. 8. Cyclizing condensation of 1H-pyrrole-3,4-dicarbaldehydes with 1,2-bifunctional compounds. A general and simple preparation method for 2H-pyrrolo[3,4-c]pyridines and 6H-pyrrolo[3,4-d]pyridazines

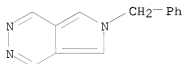
GI



AB 2H-Pyrrolo[3,4-c]pyridines I (R = CO<sub>2</sub>Me, CO<sub>2</sub>Et, cyano; R<sub>1</sub> = H, Me, CMe<sub>3</sub>, CH<sub>2</sub>Ph; R<sub>2</sub> = H, Me) are easily and efficiently accessible via reaction of 1H-pyrrole-3,4-dicarbaldehydes with H<sub>2</sub>NCH<sub>2</sub>R.HCl. Under the influence of Et<sub>2</sub>NH the cyclocondensation occurs in a uniform fashion and in 55-99% yields. In a similar manner 1H-pyrrole-3,4-dicarbaldehydes react with N<sub>2</sub>H<sub>4</sub>; two-fold elimination of H<sub>2</sub>O leads to 6H-pyrrolo[3,4-d]pyridazines.

The bicyclic hetarenes are stabilized compared with 2H-isoindoles by addnl. heteroatoms in the 6-membered ring and acceptor groups at the 6-position.

AN 1985:45802 CAPLUS <<LOGINID::20080623>>  
 DN 102:45802  
 OREF 102:7201a,7204a  
 TI Structure and reactivity of iso-fused heterocyclic systems with  $4n \pi$  and  $(4n + 2) \pi$  electrons. 8. Cyclizing condensation of 1H-pyrrole-3,4-dicarbaldehydes with 1,2-bifunctional compounds. A general and simple preparation method for 2H-pyrrolo[3,4-c]pyridines and 6H-pyrrolo[3,4-d]pyridazines  
 AU Kreher, Richard P.; Pfister, Juergen  
 CS Abt. Chem., Univ. Dortmund, Dortmund, D-4600/50, Fed. Rep. Ger.  
 SO Chemiker-Zeitung (1984), 108(9), 275-7  
 CODEN: CMKZAT; ISSN: 0009-2894  
 DT Journal  
 LA German  
 OS CASREACT 102:45802  
 IT 94169-86-5P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)  
 RN 94169-86-5 CAPLUS  
 CN 6H-Pyrrolo[3,4-d]pyridazine, 6-(phenylmethyl)- (CA INDEX NAME)

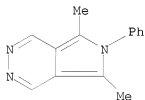


L6 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Aldehydes derived from 1,2,5-trisubstituted pyrroles  
 GI For diagram(s), see printed CA Issue.  
 AB cf. C.A. 50, 9413d. PhN.CR:CR1.CR2:CMe (I, R = Ph or Me, R1 = R2 = H) (II, III) formylated with HCONMe2 and POCl3, the corresponding aldehydes (I, R = Ph or Me, R1 = H, R2 = CHO) (IV, V) reduced, the trimethylpyrroles (I, R = Ph or Me, R1 = H, R2 = Me) (VI, VII) formylated and the aldehydes (I, R = Ph or Me, R1 = CHO, R2 = Me) (VIII, IX) again reduced yielded the completely substituted pyrroles (I, R = Ph or Me, R1 = R2 = Me) (X, XI). III also gave the dialdehyde (I, R = Me, R1 = R2 = CHO) (XII). Knorr-Paál condensation of PhNH2 with (AcCH2)2 and BzCH2CH2Ac, resp., purification of the condensation products by vacuum distillation and recrystn. (C6H12) gave II and III. III (25 g.) and 16 g. HCONMe2 in 100 ml. dry PhMe stirred well with portionwise addition of 27 g. POCl3 and the mixture heated 6 hrs. on a steam bath, shaken 20 min. with 300 ml. saturated aqueous NaOAc and extracted with PhMe, the washed (10% aqueous Na2CO3, H2O) and dried (Na2SO4) extract evaporated and the residue fractionated yielded 73% V, m. 92° (dilute MeOH), b12 190°; semicarbazone m. 294° (alc.). The residue from distillation recrystd. from alc. yielded 13% (with large excess of 3 moles HCONMe2) XII, m. 203°, giving a yellow halochromy with H2SO4. XII (1 g.) and 1 ml. N2H4.H2O refluxed 2 hrs. in alc. and the cooled mixture filtered gave 0.9 g. 1,3-dimethyl-2-phenyl-5,6-diazaisoindole, m. 288°, yellow coloration with H2SO4, an azine belonging to a group of compds. of biol. interest as potential antagonists of purine bases. XII (1 mole) treated with 2 moles PhCH2CN gave the bis(phenylacrylonitrile) derivative,

C30H23N3, m. 171° (alc.). V (8 g.) and 3 g. 95% N2H4.H2O heated 10 min. at 100° in 200 ml. (HOCH2CH2)2O and the mixture refluxed 90 min. with 3.9 g. KOH with removal of H2O, the cooled mixture acidified with dilute HCl and extracted with C6H6 yielded 86.6% VII, m. 39° (dilute MeOH), b18 140°. Similarly, 10 g. IV, 2.8 g. N2H4.H2O, and 3 g. KOH in 100 ml. (HOCH2CH2)2O yielded 87% VI, m. 79° (alc.), b12 195°, no halochromy with H2SO4. VII (11.5 g.), 6.8 g. HCONMe2, and 14.5 g. POCl3 in 100 ml. dry PhMe yielded 83.3% IX, m. 134° (MeOH); semicarbazone m. 273° (alc.). The same formylation technique applied to VI gave no aldehyde, even after heating 30 hrs. VI (5.5 g.) and 2.4 g. HCONMe2 treated portionwise with 4 g. POCl3 and the sticky violet mass heated 10 hrs. on a steam bath, the cooled mass treated with 15% aqueous NaOH and the product worked up yielded 77% VIII, m. 200° (C6H12), b17 254°; oxime m. 238-9°(alc.). VIII (6 g.), 1.4 g. N2H4.H2O, and 1.4 g. KOH in 50 ml. (HOCH2CH2)2O gave 4 g. X, m. 121° (C6H12 or AcOH). IX (5 g.), 1.7 g. N2H4.H2O and 2 g. KOH in (HOCH2CH2)2O yielded 70% XI, b12 142°, darkening rapidly on exposure to air and light, also obtained by reduction of XII. The aldehydes IV and V, with a free ortho position, reacted with PhCH2CN to give the corresponding acrylonitriles (XIII, XIV) whereas VIII and IX failed to react. V (1 mole) and 1 mole PhCH2CN in alc. refluxed 5 min. with a few drops of 5N NaOH and the cooled mixture diluted with H2O, filtered and the H2O-washed precipitate recrystd. (alc.)

gave 70% XIV,  $\alpha$ -phenyl- $\beta$ -(2,5-dimethyl-1-phenyl-3-pyrryl)acrylonitrile, m. 139°. The corresponding XIII, m. 145° (alc.), was similarly prepared from IV and PhCH2CN in alc.

AN 1960:50367 CAPLUS <<LOGINID::20080623>>  
 DN 54:50367  
 OREF 54:9884b-i  
 TI Aldehydes derived from 1,2,5-trisubstituted pyrroles  
 AU Rips, Richard; Buu-Hoi, Ng. Ph.  
 CS Univ. Paris  
 SO Journal of Organic Chemistry (1959), 24, 372-4  
 CODEN: JOCEAH; ISSN: 0022-3263  
 DT Journal  
 LA Unavailable  
 OS CASREACT 54:50367  
 IT 97476-49-8P, 6H-Pyrrolo[3,4-d]pyridazine, 5,7-dimethyl-6-phenyl-  
 RL: PREP (Preparation)  
 (preparation of)  
 RN 97476-49-8 CAPLUS  
 CN 6H-Pyrrolo[3,4-d]pyridazine, 5,7-dimethyl-6-phenyl- (CA INDEX NAME)



L6 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Friedel-Crafts acylations of 1-phenyl-2,5-dimethylpyrrole and 1,2-diphenyl-5-methylpyrrole  
 AB Friedel-Crafts acylations of 1-phenyl-2,5-dimethyl-pyrrole (I) yield diketones when acetyl (II) and propionyl chlorides (III) are used, and both mono- and diketones with BzCl (IV) and anisoyl chloride (V). On the

other hand, 1,2-diphenyl-5-methylpyrrole (VI) gave predominantly monoketones with both type of acid chlorides, substitution occurring at the 4-position. Condensation of 3,4-diacylpyrroles with N2H4.H2O led to derivs. of 5,6-diazaisoindole, a new heterocyclic nucleus analogous to purine. I (15 g.) and 14 g. AlCl3 in 200 ml. CS2 treated with 7.5 g. II portionwise, the mixture heated 2 hrs. at 40°, cooled, H2O added, washed with 5% aqueous NaOH, dried, and distilled gave 9 g.

#### 3,4-diacyl-1-phenyl-

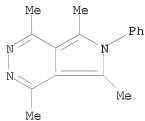
3,5-dimethylpyrrole (VII), b15 235-40°, prisms, m. 98°, yellow color with H2SO4. In an experiment in which AlCl3 was added at 0°, and the mixture kept overnight at 15°, an 18% yield VII was obtained. I (20 g.) and 10 g. II in 100 ml. dry thiophene-free C6H6 heated 2 hrs. at 50° with 36.5 g. SnCl4 gave 52% VII. VII (2.5 g.) in 10 ml. alc. was treated with 1 g. 95% N2H4.H2O; an exothermic reaction occurred, and a precipitate was collected to give 2.2 g.

#### 1,3,4,7-tetramethyl-2-

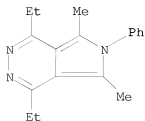
phenyl-5,6-diazaisoindole, m. 318° (MeOH), yellow color with H2SO4. I (10 g.) and 12 g. III in 100 ml. C6H6 treated with 18.2 g. SnCl4 gave 14 g. of the dione (VIII), b20 252°, silky needles, m. 66°. VIII was obtained in 25% yield when AlCl3 was used as catalyst, the reaction being performed at room temperature and in CS2. VIII (1.4 g.) and 0.5 g. N2H4.H2O in 5 ml. alc. refluxed 3 hrs. gave 1,3-dimethyl-2-phenyl-4,7-diethyl-5,6-diazaisoindole, m. 190° (aqueous MeOH). I (20 g.), 18 g. BzCl, and 37 g. SnCl2 in C6H6 gave 2 ketonic portions. The lower-boiling portion of 15 g. consisted of 3-benzoyl-1-phenyl-2,5-dimethylpyrrole, b15 260°, leaflets, m. 126°. The higher-boiling fraction of 10 g. consisted of 3,4-dibenzoyl-1-phenyl-2,5-dimethylpyrrole (IX), b17 320-30°, plates, m. 186°. A similar reaction, using the same amts. of starting materials, and performed with AlCl3 at 40° in CS2 gave 17 g. IX. IX (0.5 g.) and 0.4 g. N2H4.H2O in 5 ml. alc. gave 0.4 g. 1,3-dimethyl-1,4,7-triphenyl-5,6-diazaisoindole, yellow needles, m. 294° (alc.). I (20 g.), 22 g. V, and 16.5 g. AlCl3 at 40° in CS2 gave 2 portions, one of 5.5 g. of 3-anisoyl-1-phenyl-2,5-dimethylpyrrole (X), lustrous leaflets, m. 116°, b14 275-90°. The other portion of 15 g. consisted of 3,4-dianisoyl-1-phenyl-2,5-dimethylpyrrole (XI), b2 300°, leaflets, m. 183°. A SnCl4-catalyzed acylation using the same amts. of starting materials gave 10 g. X and 10 g. XI. 1,3-Dimethyl-1-phenyl-4,7-bis(p-methoxyphenyl)-5,6-diazaisoindole crystallized as lemon-yellow plates, m. 295° (alc.). All the acylations of VI were effected with equimolar amts. of VI and of the acid chlorides. The acetylation, performed at various temps. and with AlCl3 as well as SnCl2, gave predominantly 4-acetyl-1,2-diphenyl-5-methylpyrrole (XII), b11 240-2°, needles, m. 101-2°; oxime, prisms, m. 176° (alc.). Repeated fractional crystallization from MeOH of the higher-boiling fractions gave small amts. of 3,4-diacyl-1,2-diphenyl-5-methylpyrrole (XIII), m. 161°, yellow coloration with H2SO4. The yields of XII and XIII are recorded as follows (catalyst, temperature of reaction, and % total yield of XII and XIII given): AlCl3, 0-5°, 15; AlCl3, 18°, 38; AlCl3, 40°, 52; SnCl4, 18°, 48; SnCl4, 60°, 59. 1,2-Diphenyl-3,4,7-trimethyl-5,6-diazaisoindole crystallized as silky needles, m. 239° (aqueous alc.). VI propionylated 3 hrs. at 50° with SnCl4 gave 60% 4-propionyl-1,2-diphenyl-5-methylpyrrole (XIV), b15 254-5°, leaflets, m. 126° (alc.). No dione could be isolated from the higher-boiling fractions. With AlCl3 as catalyst at 40°, a 40% yield of XIV was obtained; semicarbazone, leaflets, m. 260° (alc.). VI with IV and SnCl4 at 50° gave 2 products; 49% 4-benzoyl-1,2-diphenyl-5-methylpyrrole, b0.3 244°, prisms, m. 131-2° (MeOH); 2,4-dinitrophenylhydrazones, prisms, m. 190° (aqueous dioxane). A 32% yield of 3,4-dibenzoyl-1,2-diphenyl-5-methylpyrrole (XV) was obtained, b0.5 above 260°, prisms, m. 200° (alc.).

With AlCl<sub>3</sub> at 40°, a 39 % yield of XV was recorded.  
 1,2,4,7-Tetraphenyl-3-methyl-5,6-diazaisoindole crystallized from alc. as lemon-yellow plates, m. 277°, golden-yellow color in H<sub>2</sub>SO<sub>4</sub>. VI with SnCl<sub>4</sub> and V at 50° gave 51% 4-anisoyl-1,2-diphenyl-5-methylpyrrole, b<sub>11</sub> 310-12°, prisms, m. 179-80° (alc.) [semicarbazone, m. 241° (alc.)], and 40% yield 3,4-dianisoyl-1,2-diphenyl-5-methylpyrrole (XVI), b<sub>0.5</sub> 300-5° (alc.), prisms, m. 208°. With AlCl<sub>3</sub> a 29% yield of XVI was obtained at 40°, and a 9% yield when the reaction was performed at room temperature 1,2-Diphenyl-3-methyl-4,7-bis(p-methoxyphenyl)-5,6-diazaisoindole obtained as yellow plates, m. 301° (alc.), deep yellow color with H<sub>2</sub>SO<sub>4</sub>. The above listed diazaisoindoles may have biol. interest as potential antipurines.

AN 1959:122015 CAPLUS <<LOGINID::20080623>>  
 DN 53:122015  
 OREF 53:21878b-i,21879a-c  
 TI Friedel-Crafts acylations of 1-phenyl-2,5-dimethylpyrrole and 1,2-diphenyl-5-methylpyrrole  
 AU Rips, Richard; Buu-Hoi, Ng. Ph.  
 CS Univ. Paris  
 SO Journal of Organic Chemistry (1959), 24, 551-4  
 CODEN: JOCEAH; ISSN: 0022-3263  
 DT Journal  
 LA Unavailable  
 OS CASREACT 53:122015  
 IT 109450-25-1P, 6H-Pyrrolo[3,4-d]pyridazine, 1,4,5,7-tetramethyl-6-phenyl- 109562-64-3P, 6H-Pyrrolo[3,4-d]pyridazine, 1,4-diethyl-5,7-dimethyl-6-phenyl-  
 RL: PREP (Preparation)  
 (preparation of)  
 RN 109450-25-1 CAPLUS  
 CN 6H-Pyrrolo[3,4-d]pyridazine, 1,4,5,7-tetramethyl-6-phenyl- (CA INDEX NAME)



RN 109562-64-3 CAPLUS  
 CN 6H-Pyrrolo[3,4-d]pyridazine, 1,4-diethyl-5,7-dimethyl-6-phenyl- (CA INDEX NAME)



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Uploading C:\Program Files\STNEXP\Queries\10520962nitrogen.str



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ring nodes :
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exact/norm bonds :
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10-11
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G1:H,C

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Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS
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L7            STRUCTURE UPLOADED

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SAMPLE SCREEN SEARCH COMPLETED -            463 TO ITERATE

100.0% PROCESSED            463 ITERATIONS

11 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:    ONLINE    \*\*COMPLETE\*\*  
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PROJECTED ANSWERS:                21 TO            417

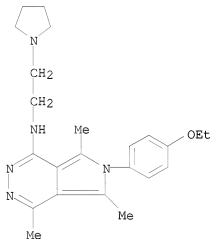
L8            11 SEA SSS SAM L7

=> d l8 scan

L8    11 ANSWERS    REGISTRY    COPYRIGHT 2008 ACS on STN

IN    6H-Pyrrolo[3,4-d]pyridazin-1-amine, 6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-  
      [2-(1-pyrrolidinyl)ethyl]-

MF    C23 H31 N5 O



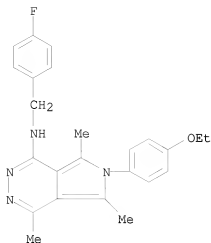
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HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

L8    11 ANSWERS    REGISTRY    COPYRIGHT 2008 ACS on STN

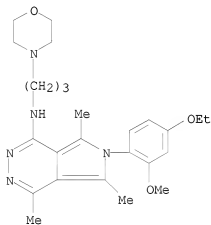
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MF    C24 H25 F N4 O



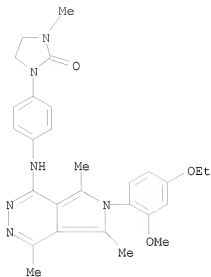
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L8 11 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN  
 IN 6H-Pyrrolo[3,4-d]pyridazin-1-amine, 6-(4-ethoxy-2-methoxyphenyl)-4,5,7-  
 trimethyl-N-[3-(4-morpholinyl)propyl]-  
 MF C25 H35 N5 O3



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L8 11 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN  
 IN 2-Imidazolidinone, 1-[4-[[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-  
 pyrrolo[3,4-d]pyridazin-1-yl]amino]phenyl]-3-methyl-  
 MF C28 H32 N6 O3



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s 17 sss full

FULL SEARCH INITIATED 17:08:32 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 9272 TO ITERATE

100.0% PROCESSED 9272 ITERATIONS

209 ANSWERS

SEARCH TIME: 00.00.01

L9

209 SEA SSS FUL L7

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

178.36

418.74

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

0.00

-8.80

FILE 'CAPLUS' ENTERED AT 17:08:36 ON 23 JUN 2008

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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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=> s l9

L10 3 L9

=> d l10 1-3 ti abs bib hitstr

L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

TI Expedited SAR study of high-affinity ligands to the  $\alpha 2\delta$   
subunit of voltage-gated calcium channels: Generation of a focused library  
using a solution-phase Sn2Ar coupling methodology

AB The SAR of the lead compound 3, a novel ligand for the  $\alpha 2\delta$   
subunit of voltage-gated calcium channels, was rapidly explored.  
Utilizing a parallel solution-phase Sn2Ar coupling approach, a focused  
library was obtained. The library was evaluated in vitro and afforded a  
series of analogs with improved potencies. The SAR trends of the library  
are also described.

AN 2005:1342000 CAPLUS <<LOGINID:20080623>>

DN 144:100381

TI Expedited SAR study of high-affinity ligands to the  $\alpha 2\delta$   
subunit of voltage-gated calcium channels: Generation of a focused library  
using a solution-phase Sn2Ar coupling methodology

AU Chen, Chixu; Stearns, Brian; Hu, Tao; Anker, Naomi; Santini, Angelina;  
Arruda, Jeannie M.; Campbell, Brian T.; Datta, Purabi; Aiyar, Jayashree;  
Munoz, Benitio

CS Department of Chemistry, Merck Research Laboratories, San Diego, CA,  
92121, USA

SO Bioorganic & Medicinal Chemistry Letters (2006), 16(3), 746-749

CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier B.V.

DT Journal

LA English

OS CASREACT 144:100381

IT 647846-36-4P 647846-47-7P 647846-73-9P

647846-77-3P 647847-24-3P 647847-35-6P

647847-43-6P 647847-44-7P 647847-47-0P

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647847-88-9P 647848-14-4P 647848-17-7P

647848-45-1P 647848-50-8P 647848-55-3P

647848-57-5P 647848-62-2P 647848-68-8P

647848-70-2P 647848-87-1P 647849-03-4P

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU  
(Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study);  
PREP (Preparation); USES (Uses)

(SAR of high-affinity ligands to  $\alpha 2\delta$  subunit of  
voltage-gated calcium channels: generation of focused library using  
solution-phase Sn2Ar coupling methodol.)

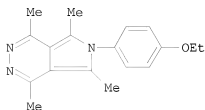
RN 647846-36-4 CAPLUS

CN 6H-Pyrrolo[3,4-d]pyridazin-1-amine, 6-(4-ethoxyphenyl)-N-1H-indol-5-yl-  
4,5,7-trimethyl- (CA INDEX NAME)

L10 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

TI Synthesis and biological evaluation of 6-aryl-6H-pyrrolo[3,4-d]pyridazine derivatives: high-affinity ligands to the  $\alpha_2\delta$  subunit of voltage gated calcium channels

GI



I

AB A novel class of 6-aryl-6H-pyrrolo[3,4-d]pyridazine ligands for the  $\alpha_2\delta$  subunit of voltage-gated calcium channels has been described. Substitutions in the aryl ring of the mol. were generally not tolerated, and resulted in diminished binding to the  $\alpha_2\delta$  subunit. Modifications to the pyridazine ring revealed numerous permissive substitutions, and detailed SAR studies were carried out in this portion of the mol. Replacement of the pyridazine ring Me group with an aminomethyl functionality provided greatly improved potency over the initial lead. The initial lead compound (I) displayed good rat pharmacokinetic properties, and was shown to be efficacious in the Chung model for neuropathic pain in rats.

AN 2004:153601 CAPLUS <<LOGINID::20080623>>

DN 140:357282

TI Synthesis and biological evaluation of 6-aryl-6H-pyrrolo[3,4-d]pyridazine derivatives: high-affinity ligands to the  $\alpha_2\delta$  subunit of voltage gated calcium channels

AU Stearns, Brian A.; Anker, Naomi; Arruda, Jeannie M.; Campbell, Brian T.; Chen, Chixu; Cramer, Merryl; Hu, Tao; Jiang, Xiaohui; Park, Kenneth; Ren, Kun Kun; Sablad, Marciano; Santini, Angelina; Schaffhauser, Herve; Urban, Mark O.; Munoz, Benito

CS Department of Medicinal Chemistry, Merck Research Laboratories, San Diego, CA, 92121, USA

SO Bioorganic & Medicinal Chemistry Letters (2004), 14(5), 1295-1298

CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier Science B.V.

DT Journal

LA English

OS CASREACT 140:357282

IT 647845-93-0P 647845-94-1P 647845-96-3P

647845-97-4P 647845-98-5P 682359-68-8P

682359-69-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

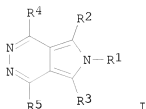
(preparation of 6-aryl-6H-pyrrolo[3,4-d]pyridazine derivs. as high-affinity ligands to the  $\alpha_2\delta$  subunit of voltage gated calcium channels)

RN 647845-93-0 CAPLUS

CN 6H-Pyrrolo[3,4-d]pyridazin-1-amine, 6-(4-ethoxyphenyl)-N,4,5,7-tetramethyl- (CA INDEX NAME)

L10 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

TI Treatment of neuropathic pain with 6H-pyrrolo[3,4-d]pyridazine compounds  
GI



AB The title compds. [I; R1 = (un)substituted alkyl(hetero)aryl, alkyl(hetero)cycloalkyl, (hetero)aryl, (hetero)cycloalkyl; R2-R5 = a bond, (un)substituted alkyl, alkyl(hetero)aryl, alkyl(hetero)cycloalkyl, (hetero)aryl, (hetero)cycloalkyl] were prepared as as ligands of voltage gated calcium channels (VGCC), useful in the treatment of neuropathic pain, and psychiatric and mood disorders such as, for example, schizophrenia, anxiety, depression, panic, and bipolar disorder, as well as in the treatment of pain, Parkinson s disease, cognitive dysfunction, epilepsy, circadian rhythm disorders, drug addiction, drug abuse, drug withdrawal and other. E.g., a multi-step synthesis of I [R1 = 4-EtOC6H4; R2-R4 = Me; R5 = 4-MeOC6H4] which produced a 65% effect after i.p. dosing at 30 mg/kg in spinal nerve ligation model of neuropathic pain in rats, was given. The pharmaceutical composition comprising the compound I is claimed.

AN 2004:60243 CAPLUS <<LOGINID::20080623>>

DN 140:111422

TI Treatment of neuropathic pain with 6H-pyrrolo[3,4-d]pyridazine compounds

IN Anker, Naomi Burke; Arruda, Jeannie M.; Campbell, Brian Thomas; Munoz, Benito; Prasit, Petpiboon; Stearns, Brian A.

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 203 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

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	EP 1539168	A2	20050615	EP 2003-764414	20030708

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	US	20060154929 A1 20060713 US 2005-520962 20051128
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	WO	2003-US21493 W 20030708
OS	MARPAT	140:111422